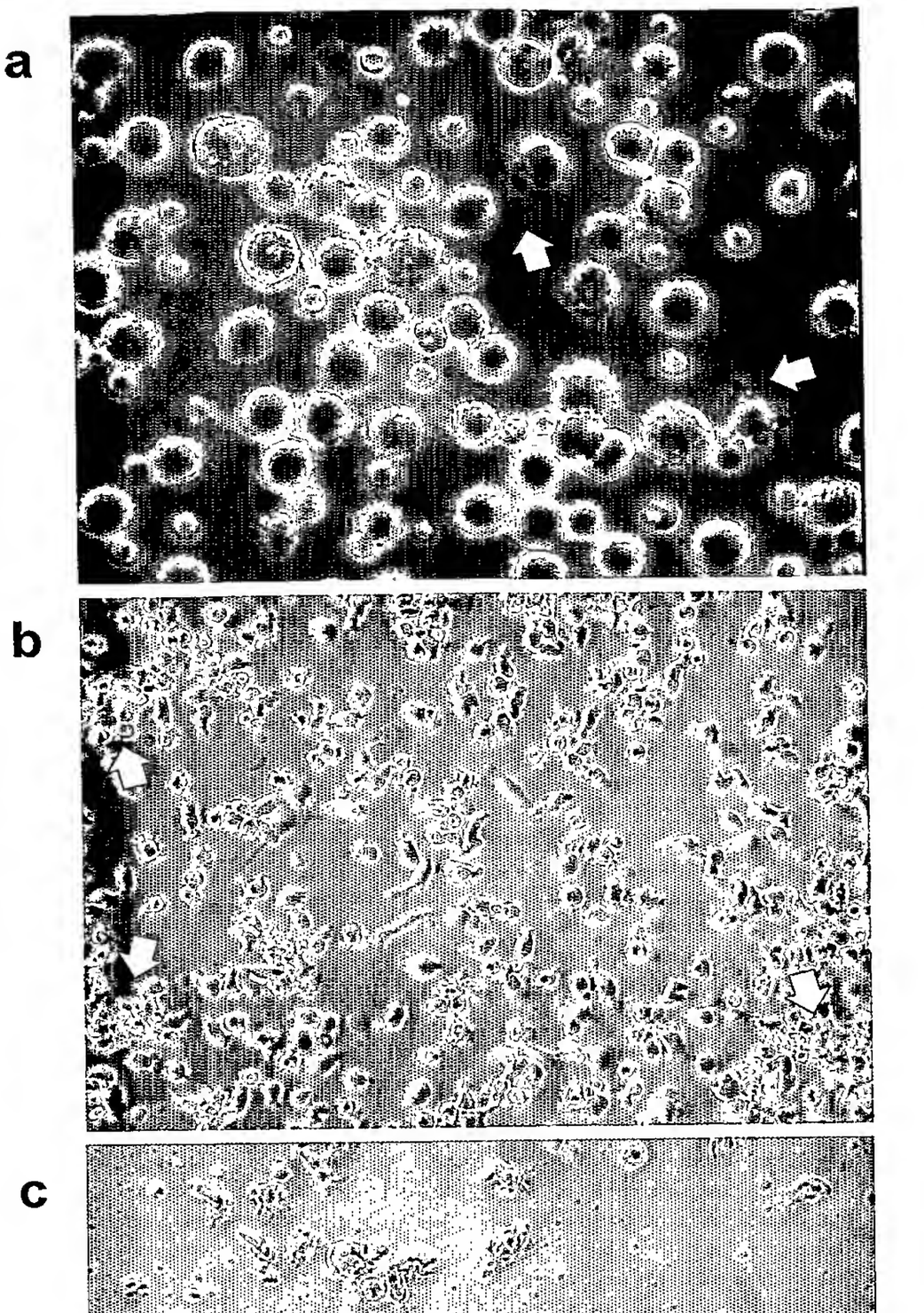
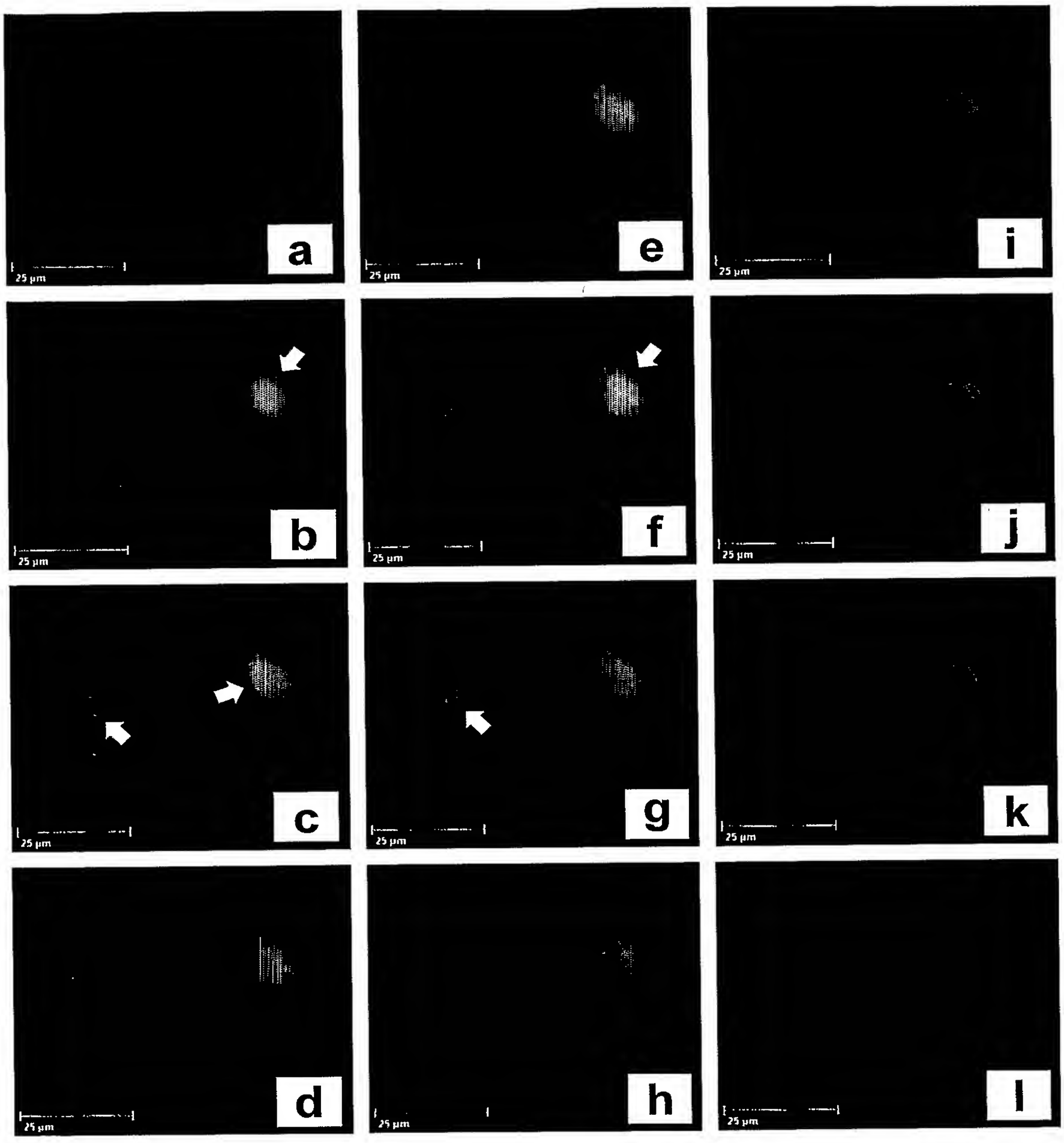


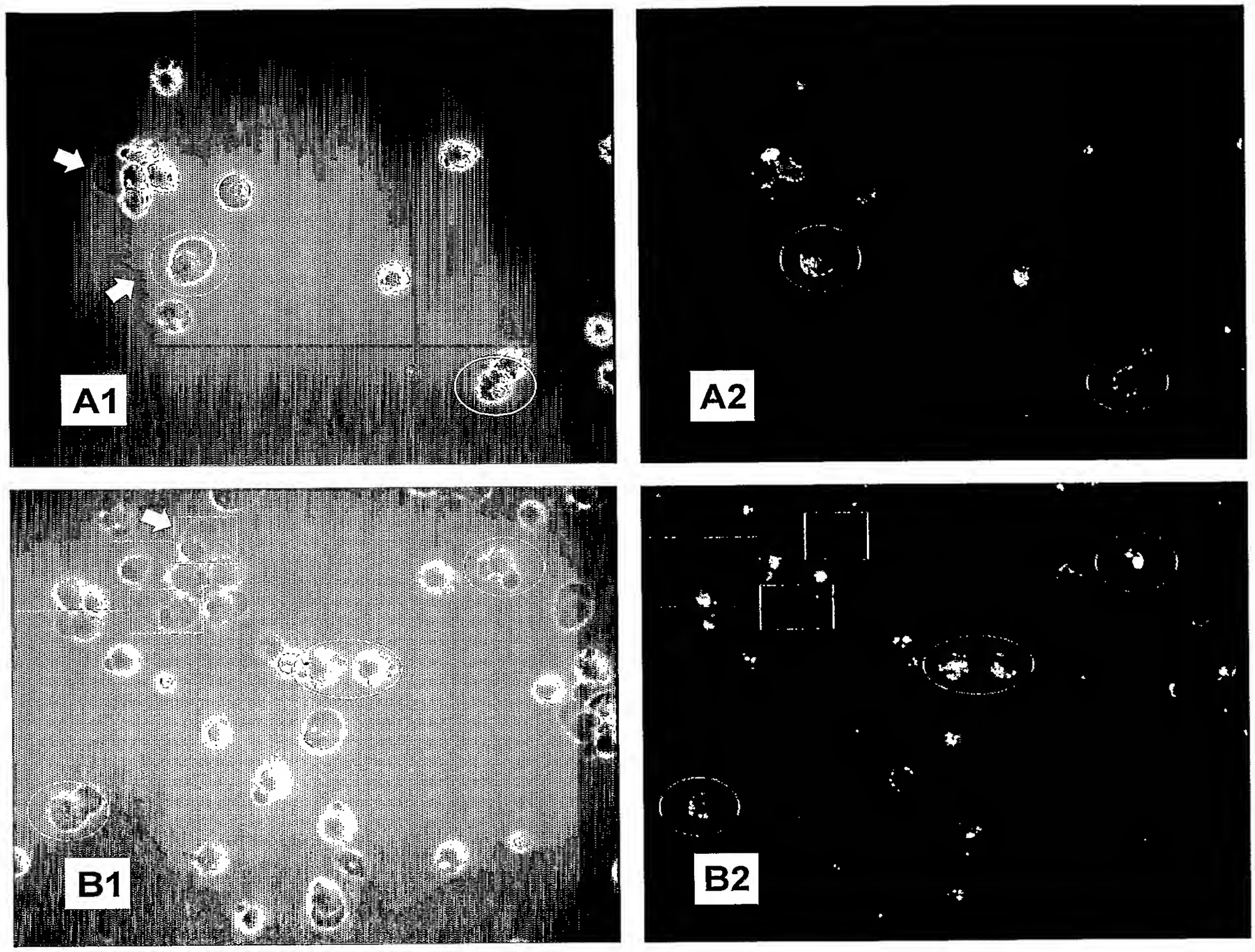
FIG. 1

Basic morphological appearance of human myeloid dendritic cells (mDCs) during differentiation *in vitro.*



Serial Optical sections through immature myeloid dendritic cells (mDCs) targeted with *fucose-labeled* liposomes delivering the tracer dye calcein.

FIG. 2



Binding and uptake of *mannose-labeled* liposomes by immature mDCs after 5 days of culture.

FIG. 3

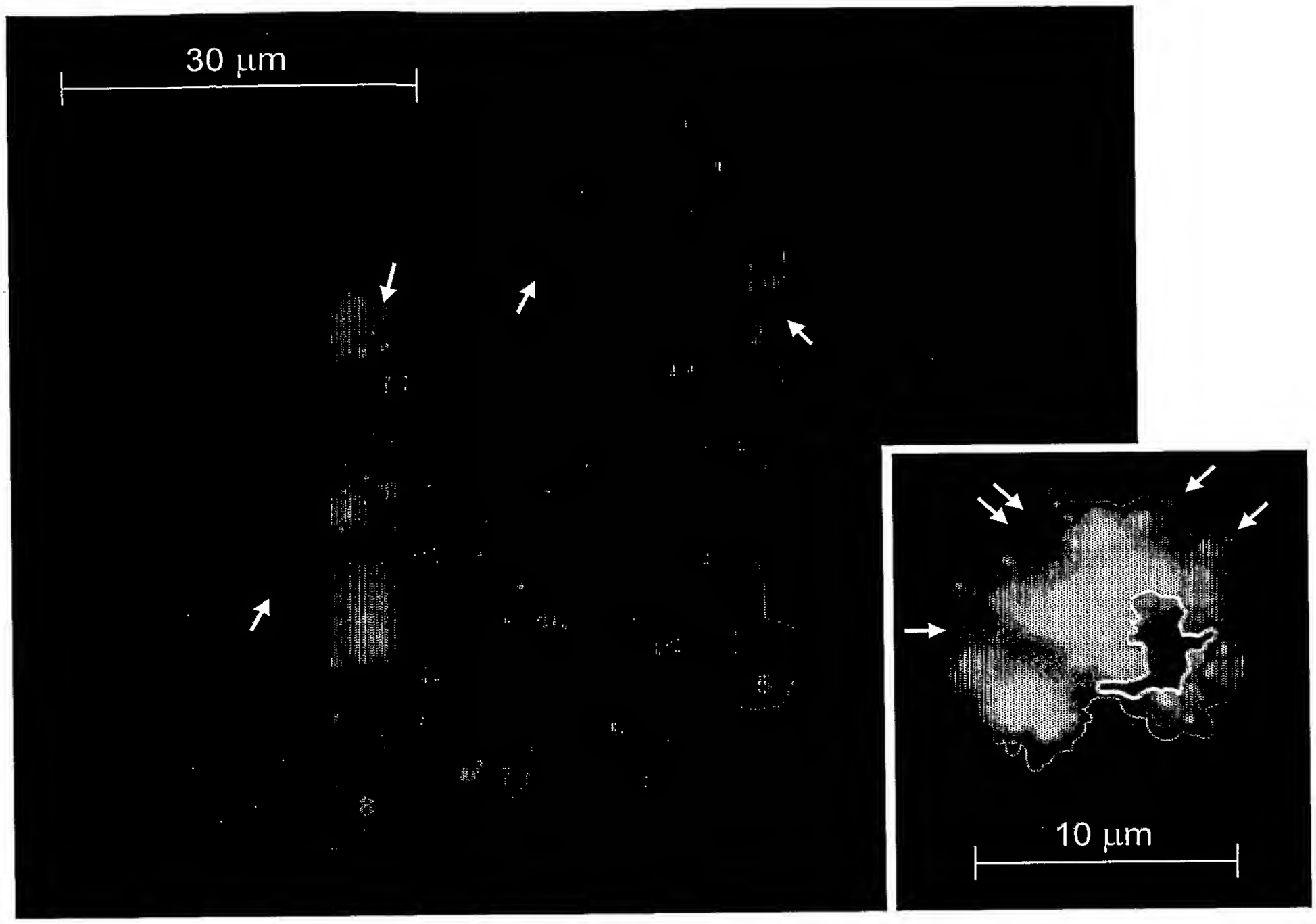
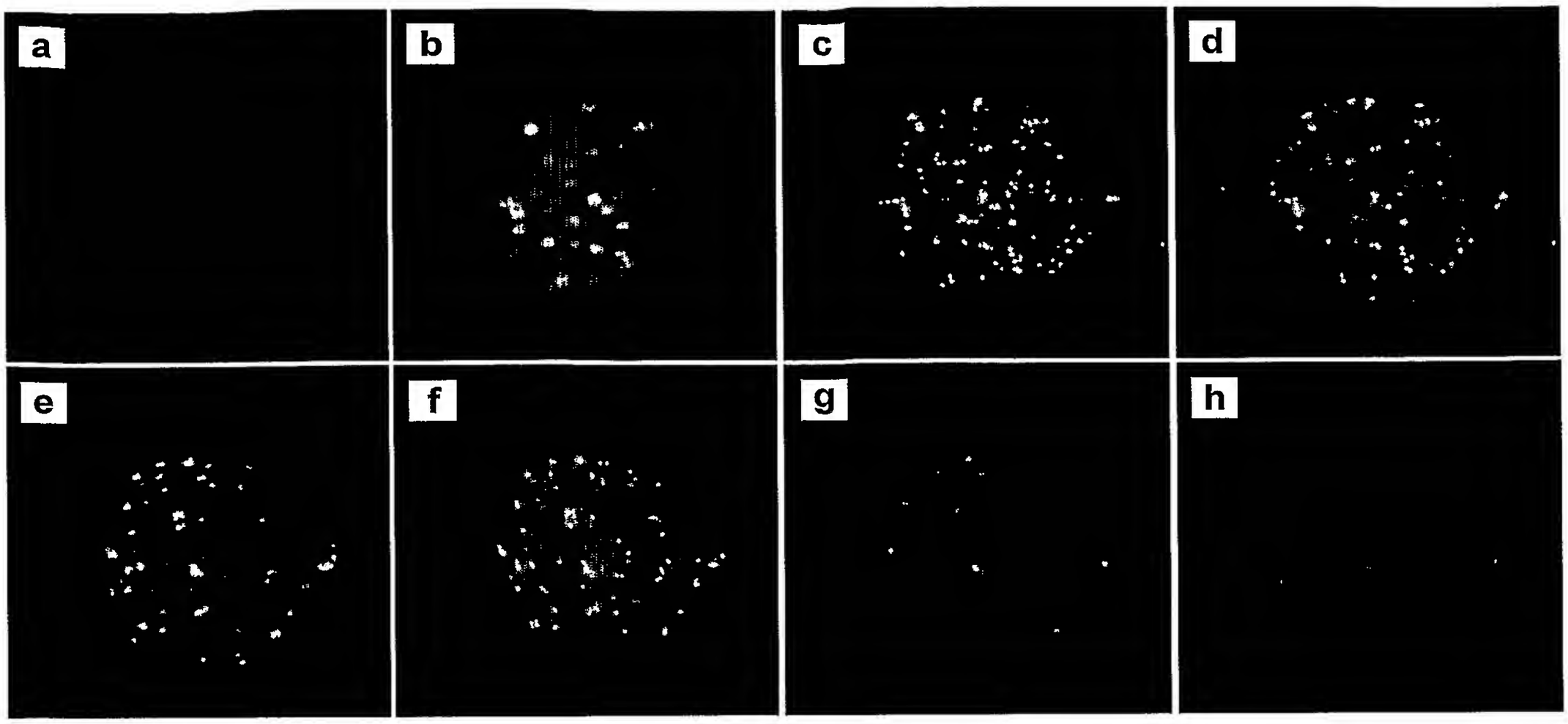


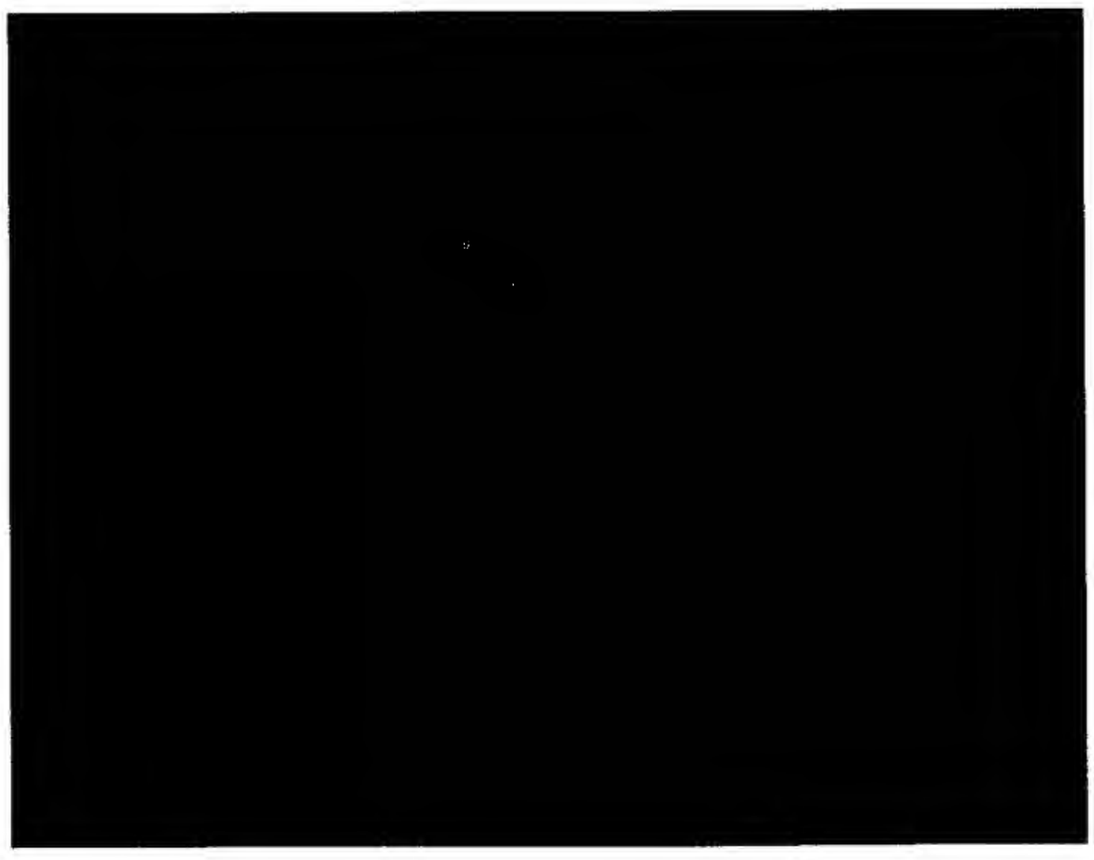
FIG. 4

C-type lectin-specific targeting of clustered mature mDCs.



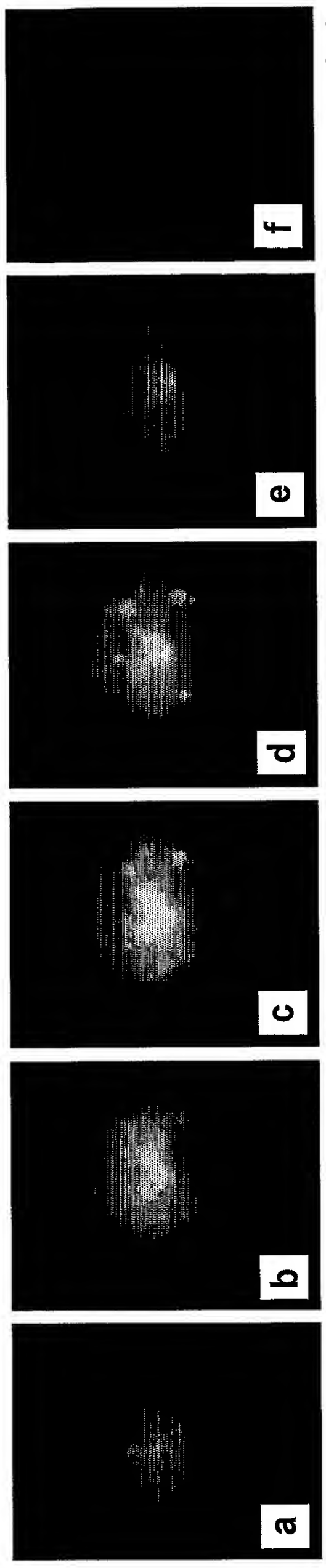
Binding and uptake of *fucose-labeled* liposomes by human macrophages after 7 days of culture.

FIG. 5



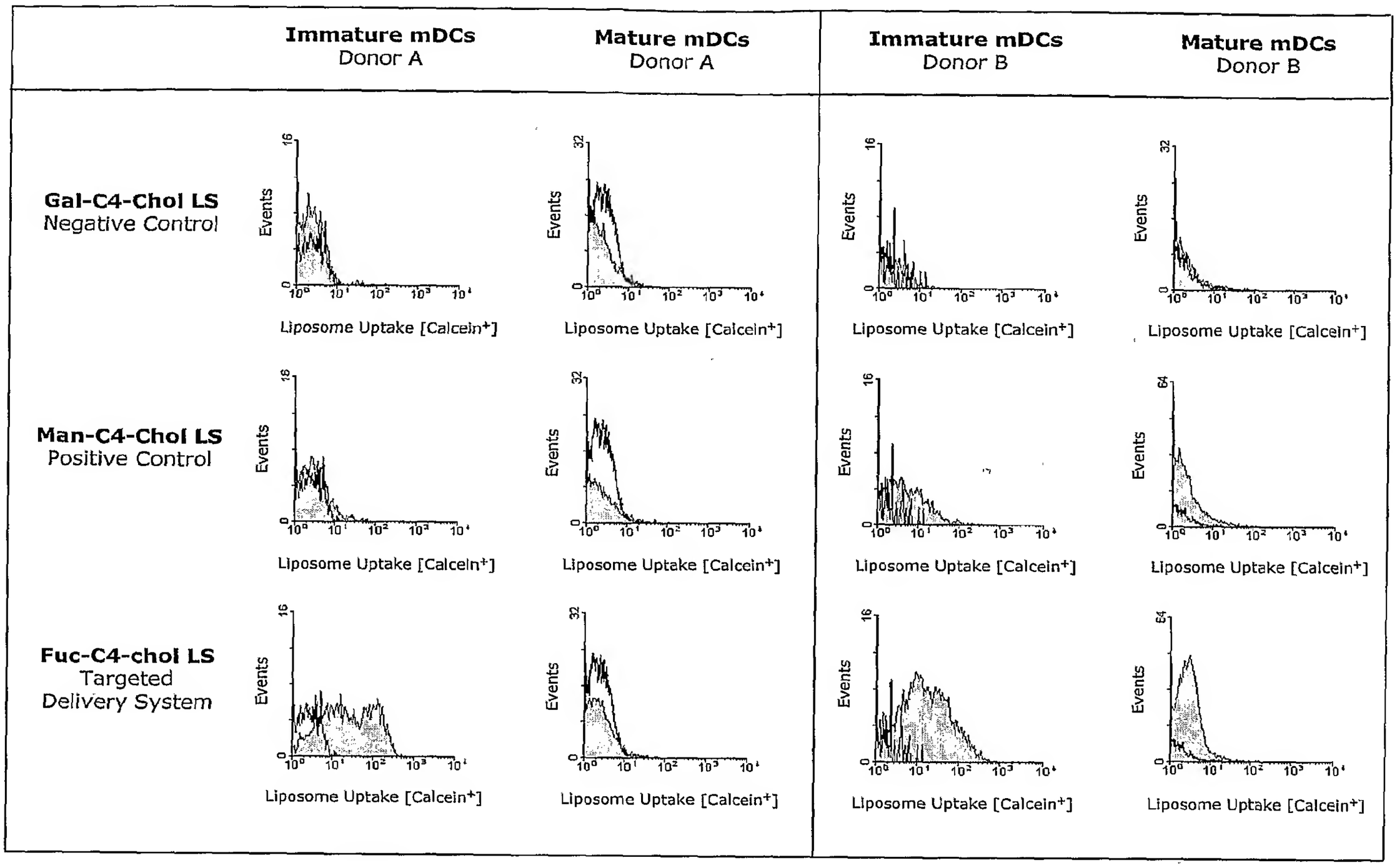
Color fluorescence photomicrograph of a representative macrophage from a different donor 2 hours after targeting with *fucose-labeled* liposomes.

FIG. 6



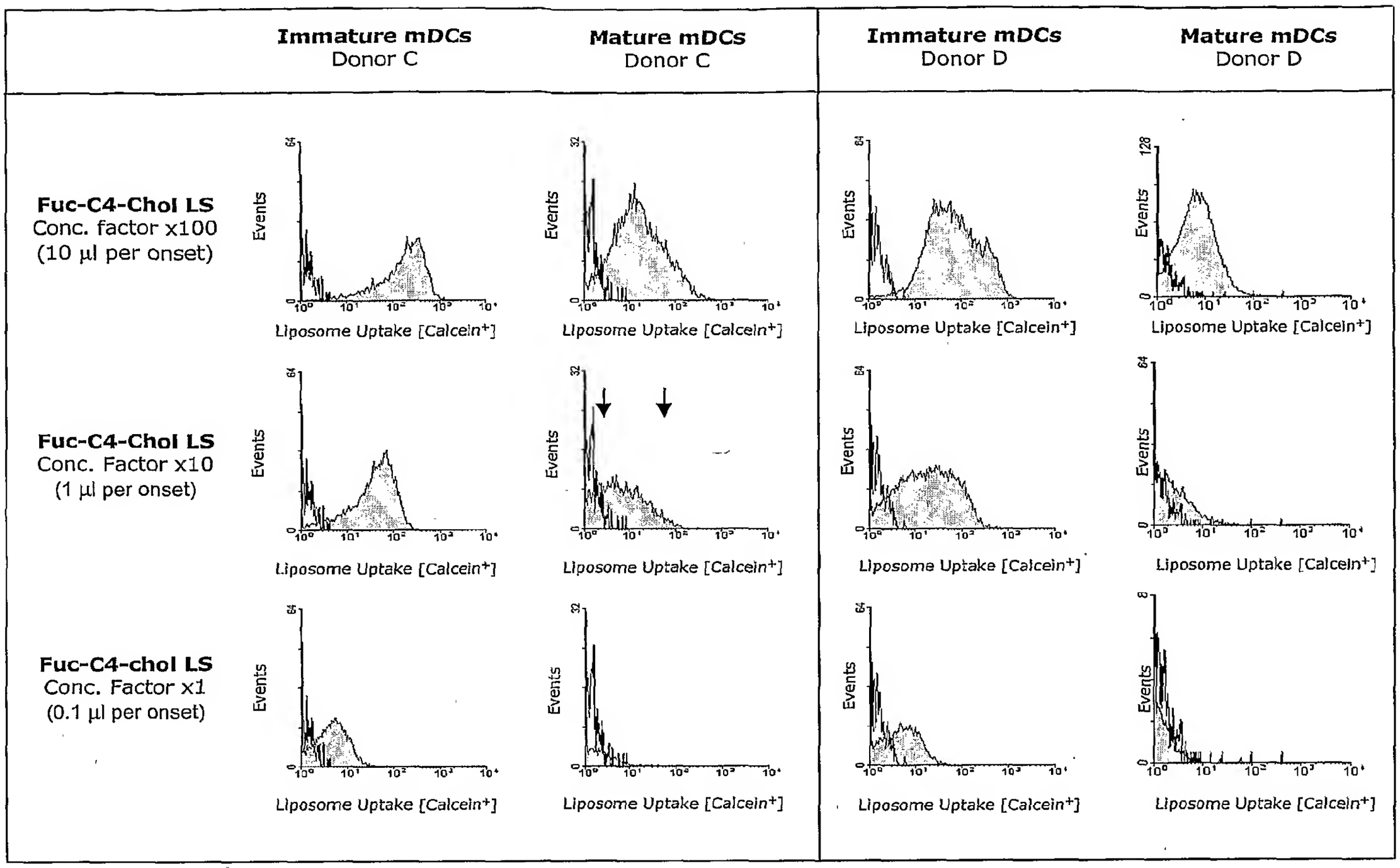
Serial optical sections through a monocyte targeted with *Fuc-4C-Chol-labeled* liposomes delivering the tracer dye calcein.

Fig. 7



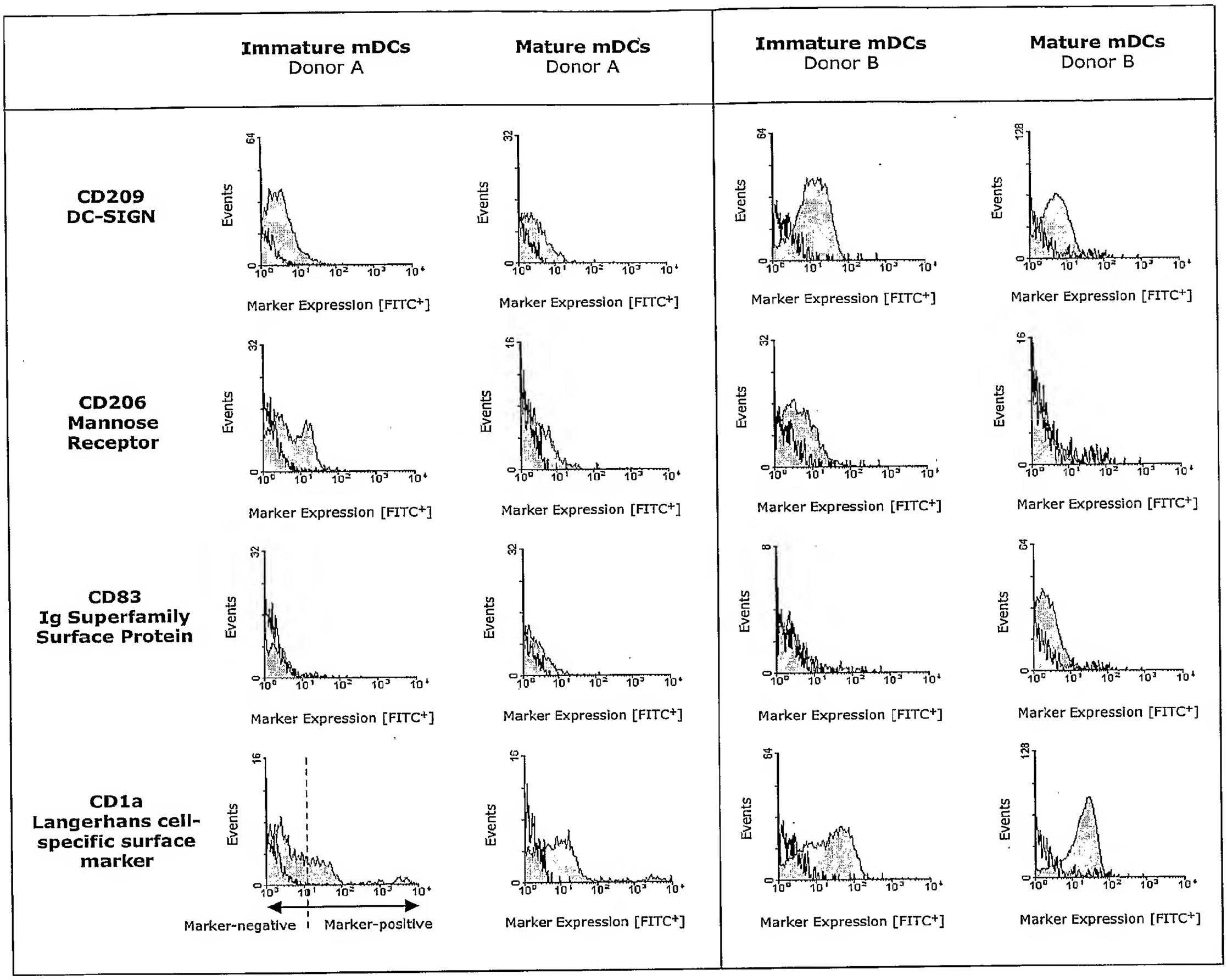
The fucose-targeted compound delivery system is highly specific and has an extremely high targeting efficacy.

FIG. 8



Increased concentrations of fucose-labeled liposomes targets both immature and mature mDCs highly efficiently.

FIG. 9



Phenotyping of immature and mature myeloid dendritic cells.

FIG. 10

FIG. 11

Morphological changes in mDCs after 8-day culture of HIV-infected mDCs upon or without targeted treatment. I.
Culture appearance and homotypic mDC clustering.

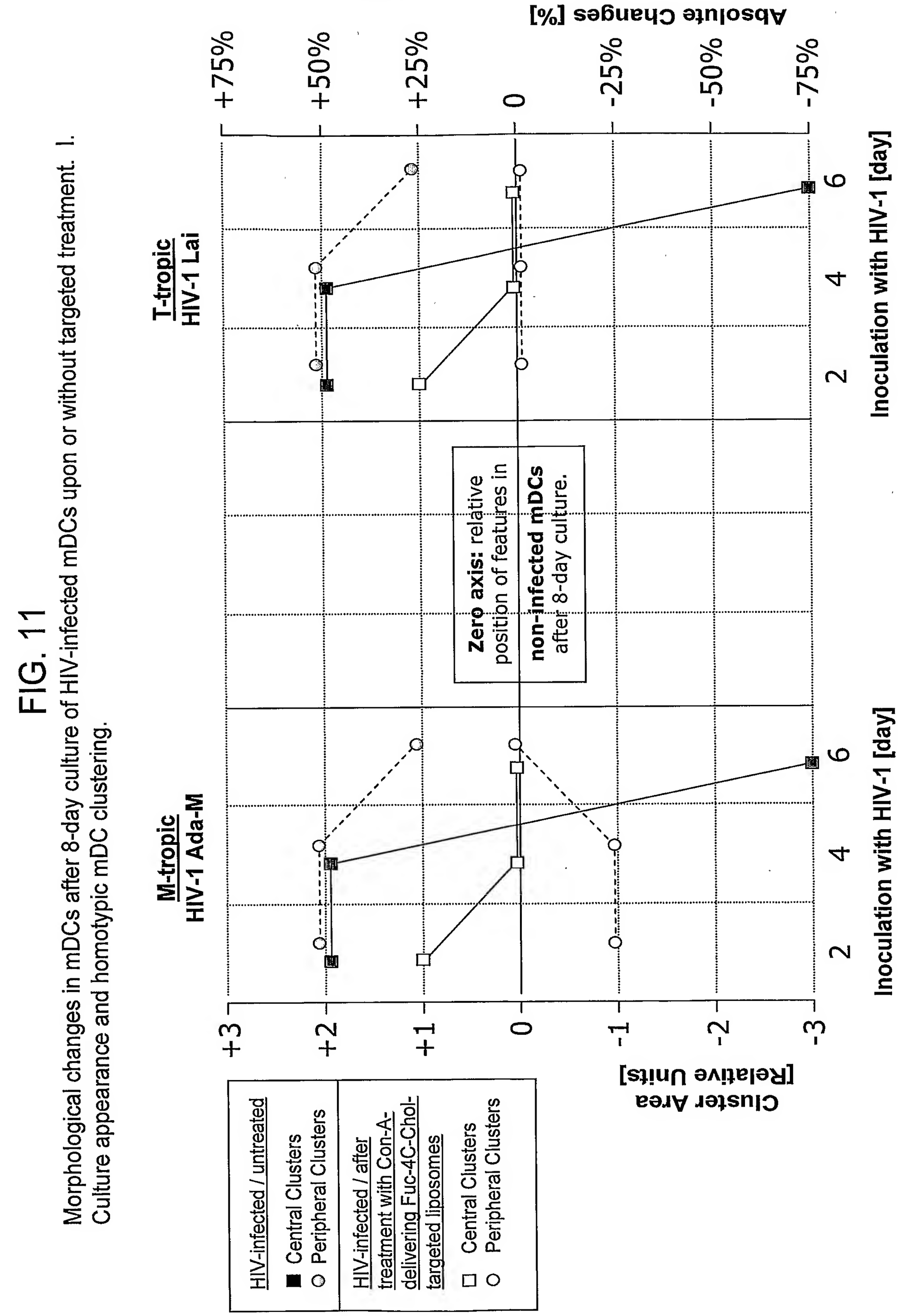


FIG. 12

Morphological changes in mDCs after 8-day culture of HIV-infected mDCs upon or without targeted treatment. II. Types of mDCs and viability.

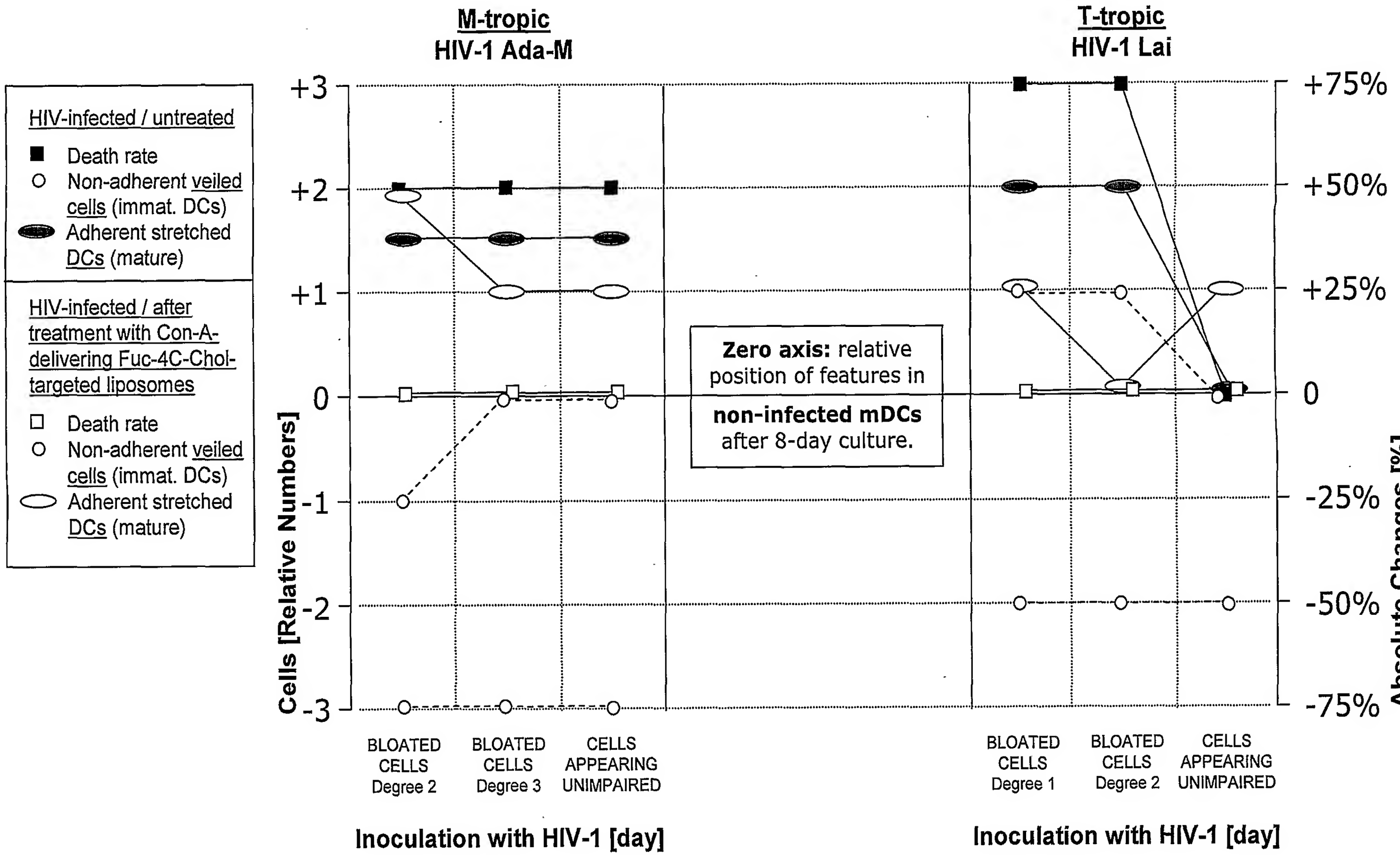
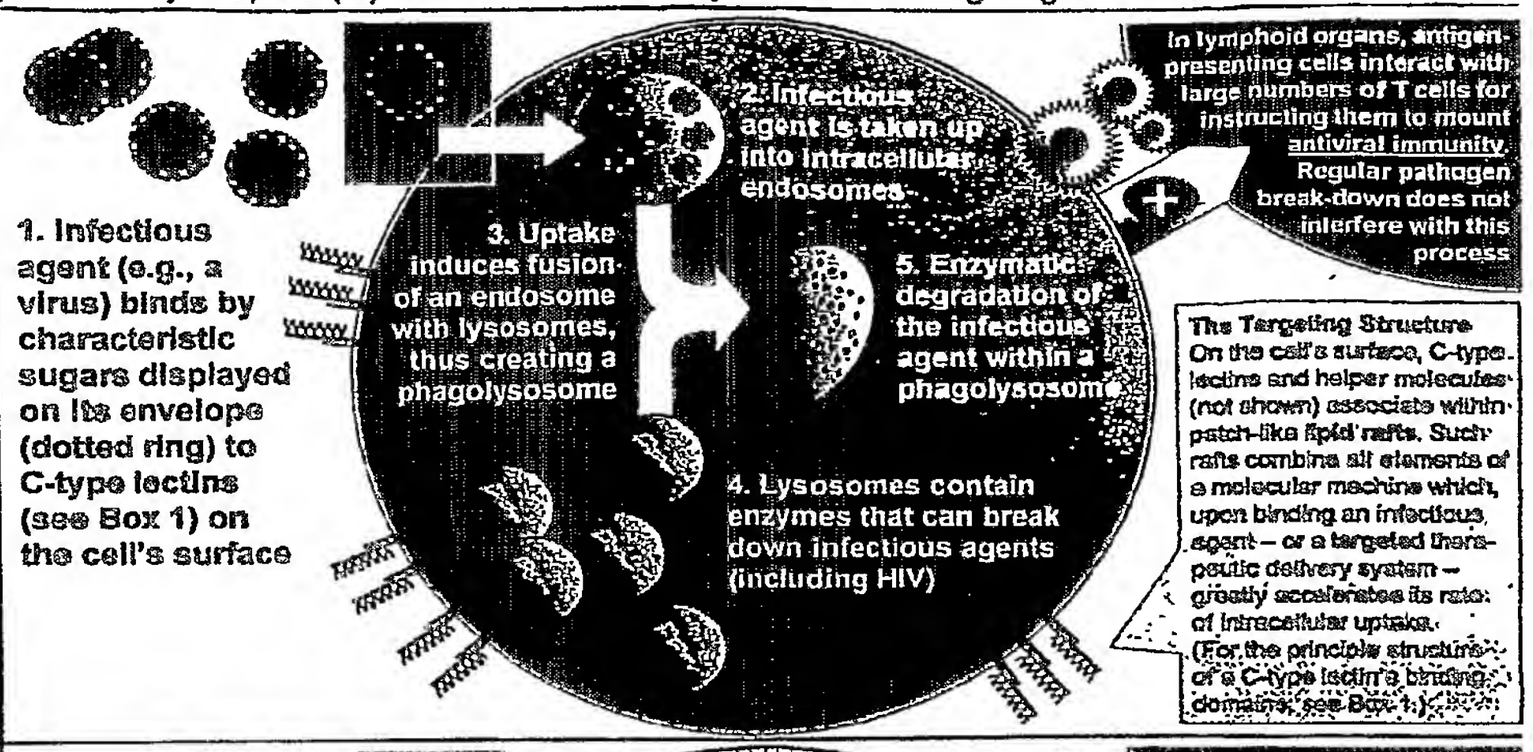


Fig. 13. (I) Normal Pathogen Elimination, (II) Evasion by HIV; and (III) The Inventive Carbohydrate-Lectin Targeting and Treatment System.

I. Normal Destruction of an Infectious Agent

In the human immune system, the first cells recognizing infectious agents are antigen-presenting cells (dendritic cells, macrophages, and others). Normally, these cells digest and dismantle infectious agents presenting their fragments to T cells for induction of specific immunity. The large circle represents such a cell, as well as key processes involved in the recognition and destruction of infectious agents. The cell section on the upper right depicts a T cell instructed for action.

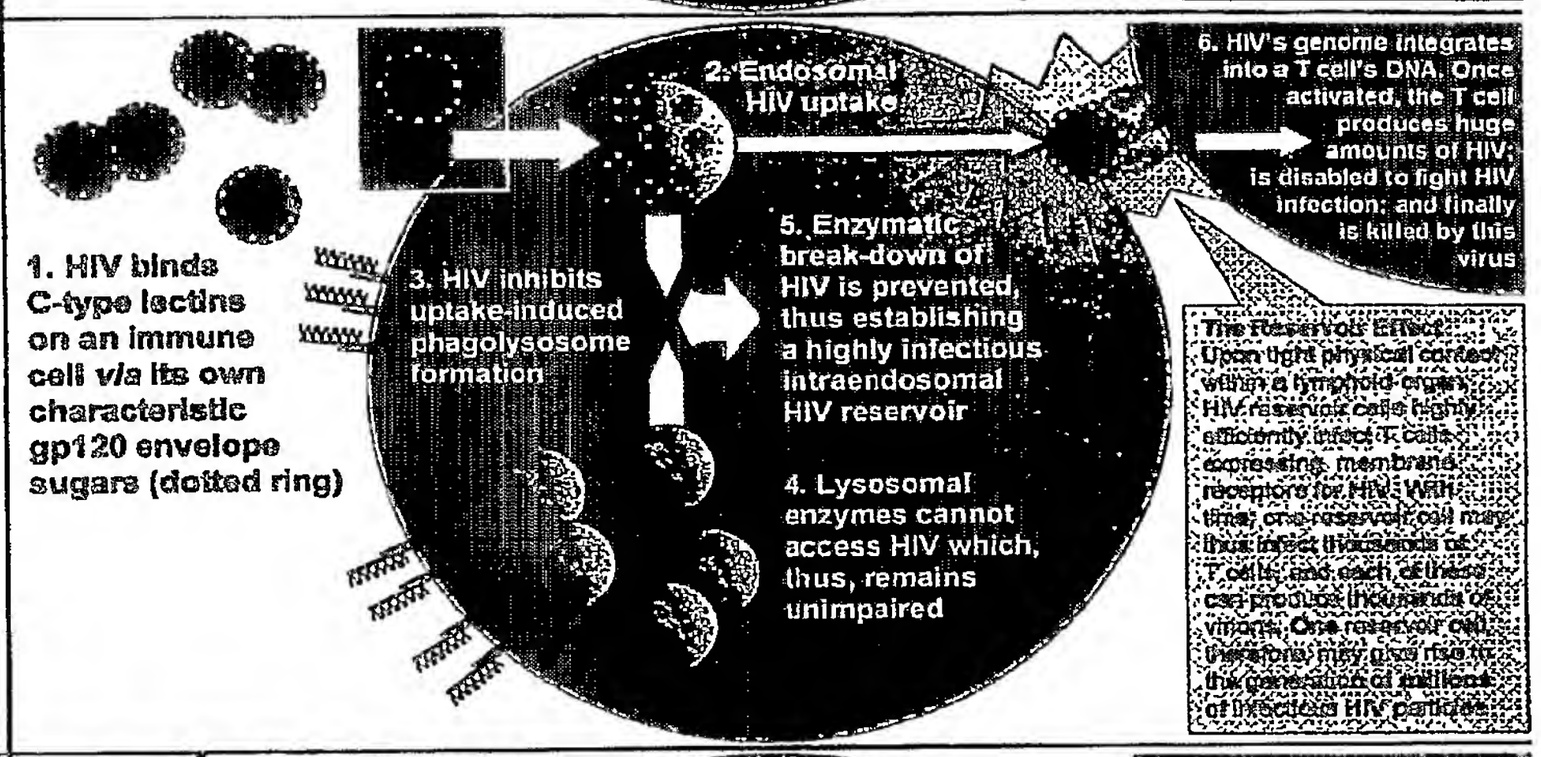


II. Evasion of Destruction by HIV and Formation of a Chronic HIV Reservoir

HIV reservoir populations can retain highly infectious virus for prolonged, yet different periods of time, i.e.,

- Days to months (dendritic cells);
- Months (follicular dendritic cells);
- Months to years (macrophages);
- Years (T-memory cells)

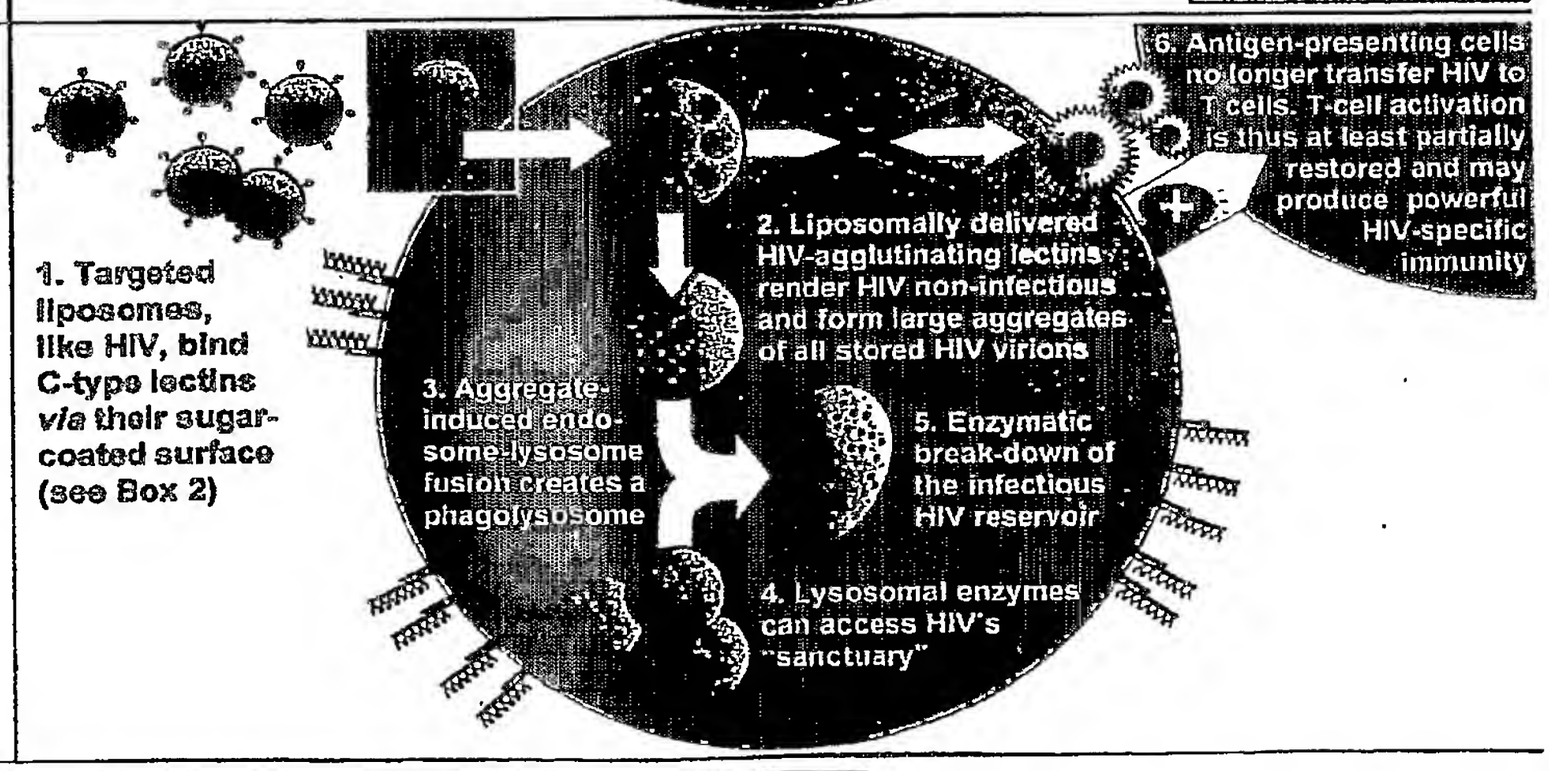
Dendritic cells, with their high turnover rate, their many physiologic subsets, and their extremely tight and frequent physical interaction with T cells, strike as the most virulent HIV reservoir when compared to the other reservoir cells.



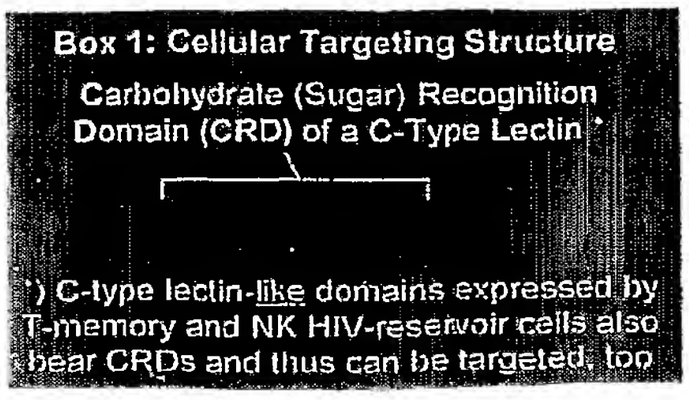
III. Elimination of the HIV Reservoir: a Two-Step Process Mediated by Carbohydrate-Lectin Interaction

1st Level:
Specific liposomal targeted delivery to the reservoir cell's surface lectins, with subsequent endosomal uptake of the liposomes;

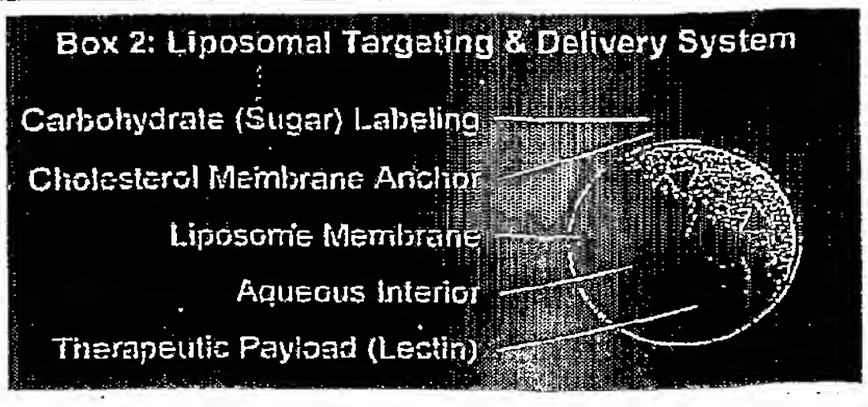
2nd Level:
Delivery of liposomally encased HIV-agglutinating lectins into the endosomes leads to the break-down of the infectious endosomal HIV reservoir



Box 1: Cellular Targeting Structure



Box 2: Liposomal Targeting & Delivery System



Note that some of the processes depicted are simplified and/or do not reflect actual sizes and ratios

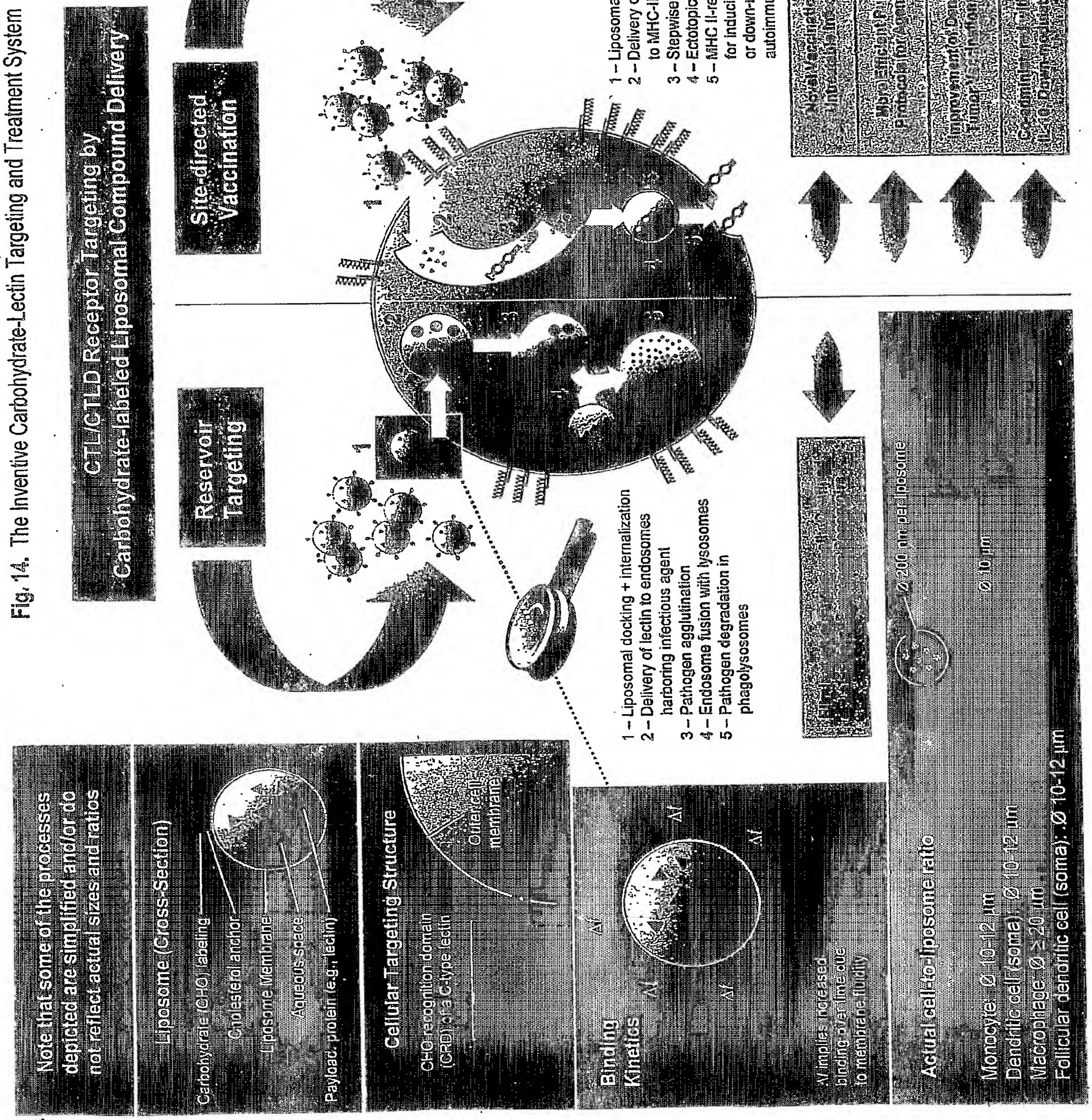


Fig. 14. The Inventive Carbohydrate-Lectin Targeting and Treatment System
CTL/C-TLD Receptor Targeting by Carbohydrate-labeled Liposomal Compound Delivery
Site-directed Vaccination
Reservoir Targeting
1 – Liposomal docking + internalization
2 – Delivery of antigenic peptides (Ag) to MHC-II processing compartment
3 – Stepwise MHC/Ag association
4 – Ectotopic vesicular transport
5 – MHC II-restricted Ag presentation for inducing protective immunity or down-modulating destructive autoimmune responses
Novel Vaccination Protocols for Intracellular Pathogens
Efficient Public Vaccination Protocols for Elimination of Tumor Cells
Improved Dendritic Cell-mediated Tumor Cell Elimination in vivo
Co-administration with cytokines (IL-10, Down-regulation of Autoimmunity)
1 – Liposomal docking + internalization
2 – Delivery of lectin to endosomes harboring infectious agent
3 – Pathogen agglutination
4 – Endosome fusion with lysosomes
5 – Pathogen degradation in phagolysosomes
Note that some of the processes depicted are simplified and/or do not reflect actual sizes and ratios
Liposome (Cross-Section)
Carbohydrate (CHO) labeling
Cholesterol anchor
Liposome Membrane
Aqueous space
Payload, protein (e.g., lectin)
Cellular Targeting Structure
CHO recognition domain (CRD) of a C-type lectin
Outer cell membrane
Binding Kinetics
Δf
Δf
Δf
Δf
Δf implies increased binding overtime due to membrane fluidity
Actual cell-to-liposome ratio
Ø 200 nm per liposome
Ø 10 mm
Monocyte: Ø 10-12 µm
Dendritic cell (soma): Ø 10-12 µm
Macrophage: Ø ≥ 20 µm
Follicular dendritic cell (soma): Ø 10-12 µm